

# Pancreatic Islet Transplantation

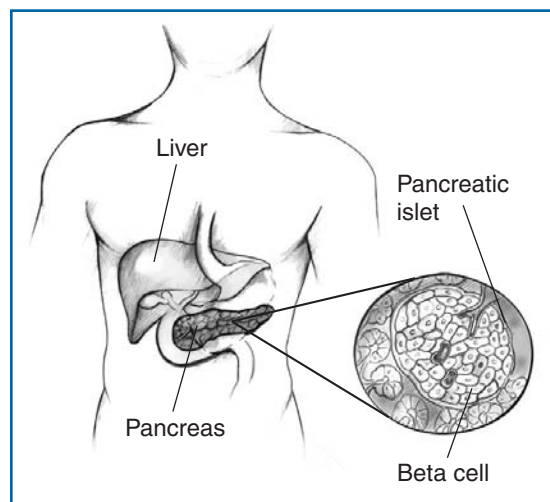
*National Diabetes Information Clearinghouse*



## What are pancreatic islets?

Pancreatic islets, also called islets of Langerhans, are tiny clusters of cells scattered throughout the pancreas. The pancreas is an organ about the size of a hand located behind the lower part of the stomach.

Pancreatic islets contain several types of cells, including beta cells, that produce the hormone insulin. The pancreas also makes enzymes that help the body digest and use food.



Pancreatic islets contain several types of cells, including beta cells, that produce the hormone insulin.

When the level of blood glucose, also called blood sugar, rises after a meal, the pancreas responds by releasing insulin into the bloodstream. Insulin helps cells throughout the body absorb glucose from the bloodstream and use it for energy.

Diabetes develops when the pancreas does not make enough insulin, the body's cells do not use insulin effectively, or both. As a result, glucose builds up in the blood instead of being absorbed by cells in the body.

In type 1 diabetes, the beta cells of the pancreas no longer make insulin because the body's immune system has attacked and destroyed them. The immune system protects people from infection by identifying and destroying bacteria, viruses, and other potentially harmful foreign substances. A person who has type 1 diabetes must take insulin daily to live. Type 2 diabetes usually begins with a condition called insulin resistance, in which the body has trouble using insulin effectively. Over time, insulin production declines as well, so many people with type 2 diabetes eventually need to take insulin.

## What is pancreatic islet transplantation?

The two types of pancreatic islet transplantation are

- allo-transplantation
- auto-transplantation

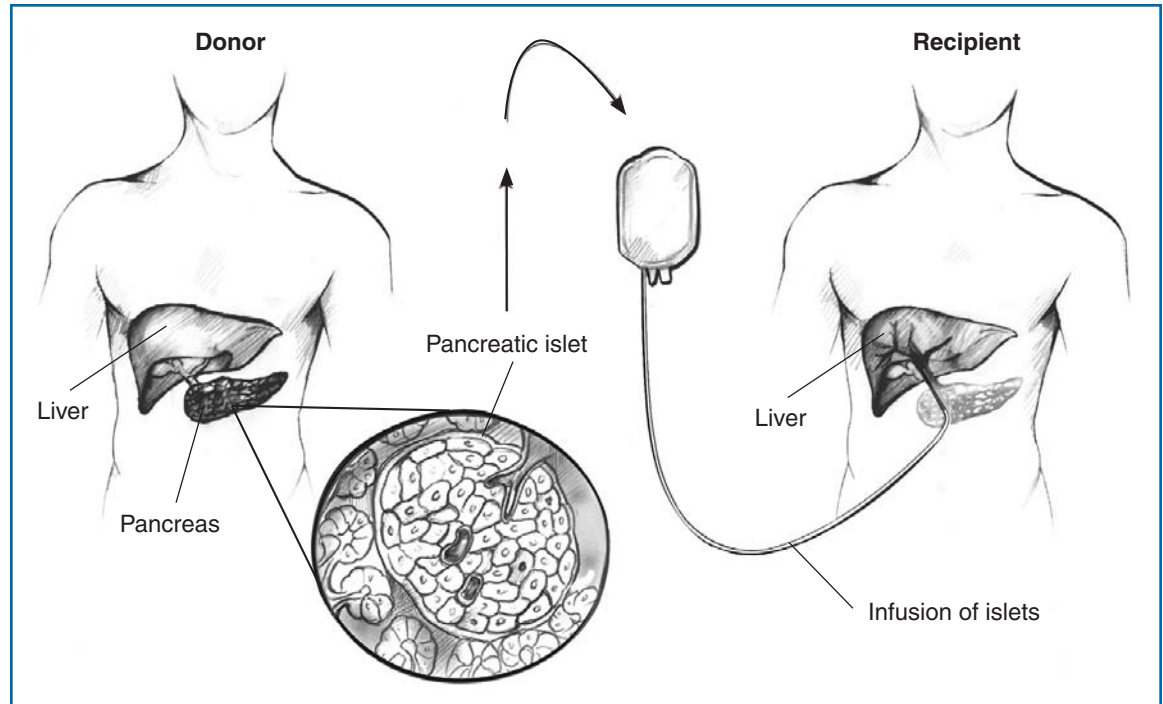
**Pancreatic islet allo-transplantation** is a procedure in which islets from the pancreas of a deceased organ donor are purified, processed, and transferred into another person. Pancreatic islet allo-transplantation is currently labeled an experimental procedure until the transplantation technology is considered successful enough to be labeled therapeutic. For more information, see the section “What are the obstacles to pancreatic islet allo-transplantation?”

For each pancreatic islet allo-transplant infusion, researchers use specialized enzymes to remove islets from the pancreas of a single, deceased donor. The islets are purified and counted in a lab. Transplant patients typically receive two infusions with an average of 400,000 to 500,000 islets per infusion. Once implanted, the beta cells in these islets begin to make and release insulin.

Pancreatic islet allo-transplantation is performed in certain patients with type 1 diabetes whose blood glucose levels are difficult to control. The goals of the transplant are to help these patients achieve normal blood glucose levels with or without daily injections of insulin and to reduce or eliminate hypoglycemia unawareness—a dangerous condition in which a person with diabetes cannot feel the symptoms of hypoglycemia, or low blood glucose. When a person feels the symptoms of hypoglycemia, steps can be taken to bring blood glucose levels back to normal.

Pancreatic islet allo-transplants are only performed at hospitals that have received permission from the U.S. Food and Drug Administration (FDA) for clinical research on islet transplantation. The transplants are often performed by a radiologist—a doctor who specializes in medical imaging. The radiologist uses x rays and ultrasound to guide the placement of a thin, flexible tube called a catheter through a small incision in the upper abdomen—the area between the chest and hips—and into the portal vein of the liver. The portal vein is the major vein that supplies blood to the liver. The islets are then infused, or pushed, slowly into the liver through the catheter. Usually, the patient receives a local anesthetic and a sedative. In some cases, a surgeon performs the transplant using general anesthesia.

Patients often need two or more transplants to get enough functioning islets to stop or reduce their need for insulin injections.



Pancreatic islet allo-transplantation (above). In islet auto-transplantation, the islets are extracted from the patient's own pancreas.

**Pancreatic islet auto-transplantation** is performed following total pancreatectomy—the surgical removal of the whole pancreas—in patients with severe and chronic, or long lasting, pancreatitis that cannot be managed by other treatments. This procedure is not considered experimental. Patients with type 1 diabetes cannot receive pancreatic islet auto-transplantation. The procedure is performed in a hospital, and the patient receives general anesthesia. The surgeon first removes the pancreas and then extracts and purifies islets from the pancreas. Within hours, the islets are infused through a catheter into the patient's liver. The goal is to give the body enough healthy islets to make insulin.

## What happens after pancreatic islet transplantation?

Pancreatic islets begin to release insulin soon after transplantation. However, full islet function and new blood vessel growth from the new islets take time. Transplant recipients usually take insulin injections until the islets are fully functional. They may also receive various medications before and after transplantation to promote successful implantation and long-term functioning of the islets. However, the autoimmune response that destroyed transplant recipients' own islets in the first place can happen again and attack the transplanted islets. Although the liver has been the traditional site for infusing the donor islets, researchers are investigating alternative sites, such as muscle tissue or another organ.

## What are the benefits and risks of pancreatic islet allo-transplantation?

The benefits of pancreatic islet allo-transplantation include improved blood glucose control, reducing or eliminating the need for insulin injections to control diabetes, and preventing hypoglycemia. An alternative to islet transplantation is whole organ pancreas transplantation that is performed most often with kidney transplantation. The advantages of whole organ pancreas transplantation are less dependence on insulin and longer duration of organ function. The main disadvantage is that a whole organ transplant is a major surgery that involves a greater risk of complications and even death.

Pancreatic islet allo-transplantation can also help reverse hypoglycemia unawareness. Research has shown that even partial islet function after a transplant can eliminate hypoglycemia unawareness.

Improved blood glucose control from a successful allo-transplant may also slow or prevent the progression of diabetes problems, such as heart disease, kidney disease, and nerve or eye damage. Research to evaluate this possibility is ongoing.

The risks of pancreatic islet allo-transplantation include the risks associated with the transplant procedure—particularly bleeding and blood clots. The transplanted islets may not function well or may stop functioning entirely. Other risks are the side effects from the immunosuppressive medications that transplant recipients must take to stop the immune system from rejecting the transplanted islets. When a patient has received a kidney transplant and is already taking immunosuppressive medications, the only additional risks are the islet infusion and the side effects from the immunosuppressive medications given at the time of allo-transplantation. Immunosuppressive medications are not needed in the case of an auto-transplant because the infused cells come from the patient's own body. Read more in the section “What is the role of immunosuppressive medications?”

## Collaborative Islet Transplant Registry Data

In its 2010 annual report,<sup>1</sup> the Collaborative Islet Transplant Registry presented data on 571 patients who received pancreatic islet allo-transplants between 1999 and 2009.

Although most procedures were pancreatic islet allo-transplants alone, 90 procedures were done in conjunction with a kidney transplant. The majority of the islet transplant patients received one or two infusions of islets; at the end of the decade, the average number of islets received per infusion was 463,000.

According to the report, about 60 percent of transplant recipients achieved insulin independence—defined as being able to stop insulin injections for at least 14 days—during the year following transplantation.

By the end of the second year, 50 percent of recipients were able to stop taking insulin for at least 14 days. However, long-term insulin independence is difficult to maintain, and eventually most recipients needed to start taking insulin again.

The report identified factors linked to better outcomes for recipients, including

- age—35 years or older
- lower pre-transplant triglyceride, or blood fat, levels
- lower pre-transplant insulin use

The report noted that even partial function of the transplanted islets can improve blood glucose control and reduce the amount of insulin needed after loss of insulin independence.

---

<sup>1</sup>Collaborative Islet Transplant Registry seventh annual report. Collaborative Islet Transplant Registry website. [https://web.emmes.com/study/isl/reports/01062012\\_7thAnnualReport.pdf](https://web.emmes.com/study/isl/reports/01062012_7thAnnualReport.pdf). Updated December 30, 2011. Accessed July 23, 2013.

## What is the role of immunosuppressive medications?

Immunosuppressive medications are needed to prevent rejection—a common problem with any transplant.

Scientists have made many advances in islet transplantation in recent years. In 2000, islet transplantation researchers at the University of Alberta in Edmonton, Canada, reported their findings in the *New England Journal of Medicine*. Their transplant protocol, known as the Edmonton protocol, has since been adapted by transplant centers around the world and continues to be refined.

The Edmonton protocol introduced the use of a new combination of immunosuppressive medications, also called anti-rejection medications, including daclizumab (Zenapax), sirolimus (Rapamune), and tacrolimus (Prograf). Researchers continue to develop and study modifications to the Edmonton protocol, including improved medication regimens that promote successful transplants. Medication regimens vary from one transplant center to another. Examples of other immunosuppressive medications used in islet transplantation include anti-thymocyte globulin (Thymoglobulin), alemtuzumab (Campath), basiliximab (Simulect), belatacept (Nulojix), etanercept (Enbrel), everolimus (Zortress), and mycophenolate mofetil (CellCept, Myfortic). Researchers are also evaluating nonimmunosuppressive medications, such as exenatide (Byetta) and sitagliptin (Januvia).

Immunosuppressive medications have significant side effects, and their long-term effects are still not fully known. Immediate side effects may include mouth sores and gastrointestinal problems, such as upset stomach and diarrhea. Patients may also have

- increased blood cholesterol, or blood fat, levels
- high blood pressure
- anemia, a condition in which red blood cells are fewer or smaller than normal, which prevents the body's cells from getting enough oxygen
- fatigue
- decreased white blood cell counts
- decreased kidney function
- increased susceptibility to bacterial and viral infections

Taking immunosuppressive medications also increases the risk of developing certain tumors and cancers.

Scientists are seeking ways to achieve immune tolerance of the transplanted islets, in which the patient's immune system no longer recognizes the islets as foreign. Immune tolerance would allow patients to maintain transplanted islets without long-term use of immunosuppressive medications. For example, one approach is to transplant islets encapsulated with a special coating, which may help to prevent rejection.

## What are the obstacles to pancreatic islet allo-transplantation?

The shortage of islets from donors is a significant obstacle to widespread use of pancreatic islet allo-transplantation. According to the Organ Procurement and Transplantation Network, in 2011 there were about 8,000 deceased organ donors available in the United States.<sup>2</sup> However, only 1,562 pancreases were recovered from donors in 2011.<sup>2</sup> Also, many donated pancreases are not suitable for extracting islets for transplants because they do not meet the selection criteria, and islets are often damaged or destroyed during processing. Therefore, only a small number of islet transplants can be performed each year.

Researchers are pursuing various approaches to solve this shortage of islets, such as transplanting islets from a single, donated pancreas, using only a portion of the pancreas from a living donor, or using islets from pigs. Researchers have transplanted pig islets into other animals, including monkeys, by encapsulating the islets with a special coating or by using medications

to prevent rejection. Another approach is creating islets from other types of cells, such as stem cells. New technologies could then be employed to grow islets in the lab.

Financial barriers also prevent the widespread use of islet allo-transplantation. Until the transplantation technology is considered successful enough to be labeled therapeutic rather than experimental, the costs of islet allo-transplants must be covered by research funds. Health insurance companies and Medicare generally do not cover experimental procedures. Federal law also does not allow health care providers or hospitals to charge patients or health insurance companies for research procedures. Some patient advocates and islet researchers feel that islet allo-transplantation is close to having a therapeutic label. The National Institutes of Health (NIH) currently supports studies that are working toward obtaining FDA licensure to reclassify islet allo-transplantation as therapeutic. In other countries, such as Canada and Scandinavia, islet allo-transplantation is no longer considered experimental and is an accepted therapy in certain patients.

---

<sup>2</sup>National data. Organ Procurement and Transplantation Network website. <http://optn.transplant.hrsa.gov/latestData/step2.asp>. Accessed July 23, 2013.



## Eating, Diet, and Nutrition

A person who receives a pancreatic islet transplant should follow a meal plan worked out with a health care provider and dietitian. Immunosuppressive medications taken

after the transplant can cause changes in a person's body, such as weight gain. A healthy diet after the transplant is important to control weight gain, blood pressure, blood cholesterol, and blood glucose levels.

### Points to Remember

- Pancreatic islets, also called islets of Langerhans, are tiny clusters of cells scattered throughout the pancreas. Pancreatic islets contain several types of cells, including beta cells, that produce the hormone insulin. Insulin helps cells throughout the body absorb glucose from the bloodstream and use it for energy.
- Pancreatic islet allo-transplantation is a procedure in which islets from the pancreas of a deceased organ donor are purified, processed, and transferred into another person.
- Pancreatic islet allo-transplantation is performed in certain patients with type 1 diabetes whose blood glucose levels are difficult to control. The goals of the transplant are to help these patients achieve normal blood glucose levels with or without daily injections of insulin and to reduce or eliminate hypoglycemia unawareness.
- Pancreatic islet auto-transplantation is performed following total pancreatectomy in patients with severe and chronic pancreatitis that cannot be managed by other treatments. This procedure is not considered experimental. Patients with type 1 diabetes cannot receive pancreatic islet auto-transplantation.
- The shortage of islets from donors is a significant obstacle to widespread use of pancreatic islet allo-transplantation. Financial barriers also prevent the widespread use of islet allo-transplantation. Until the transplantation technology is considered successful enough to be labeled therapeutic rather than experimental, the costs of islet allo-transplants must be covered by research funds.



## Hope through Research

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports research related to diabetes and many other diseases. The NIDDK conducts research in its own labs and supports basic and clinical research in medical centers and hospitals throughout the United States.

The NIDDK supports several programs related to pancreatic islet transplantation research:

- **Clinical Islet Transplantation Consortium.** Members of this consortium, which includes transplant centers from Canada, Sweden, and the United States, conduct studies of islet transplantation in patients with type 1 diabetes. For more information, visit [www.citisletstudy.org](http://www.citisletstudy.org).
- **Collaborative Islet Transplant Registry.** This registry compiles data from islet transplants in Europe, Australia, and North America and issues an annual report. For more information, visit [www.citregistry.org](http://www.citregistry.org).
- **Integrated Islet Distribution Program.** This program works with the leading islet isolation centers in the United States to distribute high-quality human islets to the diabetes research community. For more information, visit <http://iidp.coh.org>.

Studies supported by the NIDDK have investigated the use of different combinations of medications in islet transplantation and the efficacy of islets after kidney transplantation.

The NIDDK also established and supports the Beta Cell Biology Consortium. This consortium seeks to advance understanding of pancreatic islet development and function, with the goal of developing innovative therapies to correct the loss of beta cell mass in diabetes, including cell reprogramming, regeneration, and replacement.

Clinical trials are research studies involving people. Clinical trials look at safe and effective new ways to prevent, detect, or treat disease. Researchers also use clinical trials to look at other aspects of care, such as improving the quality of life for people with chronic illnesses. To learn more about clinical trials, why they matter, and how to participate, visit the NIH Clinical Research Trials and You website at [www.nih.gov/health/clinicaltrials](http://www.nih.gov/health/clinicaltrials). For information about current studies, visit [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov).

For more information about the NIDDK's research on diabetes and related topics, see [www.diabetes.niddk.nih.gov/diabetesresearch/dm\\_research.aspx](http://www.diabetes.niddk.nih.gov/diabetesresearch/dm_research.aspx).

## For More Information

**American Association of Diabetes Educators**  
200 West Madison Street, Suite 800  
Chicago, IL 60606  
Phone: 1-800-338-3633  
Internet: [www.diabeteseducator.org](http://www.diabeteseducator.org)

**American Diabetes Association**  
1701 North Beauregard Street  
Alexandria, VA 22311  
Phone: 1-800-DIABETES (1-800-342-2383)  
Email: [askADA@diabetes.org](mailto:askADA@diabetes.org)  
Internet: [www.diabetes.org](http://www.diabetes.org)

**Clinical Islet Transplantation Consortium**  
Internet: [www.citistletstudy.org](http://www.citistletstudy.org)

**Clinical Islet Transplantation Study**  
Internet: [www.isletstudy.org](http://www.isletstudy.org)

**Collaborative Islet Transplant Registry**  
Internet: [www.citregistry.org](http://www.citregistry.org)

**Immune Tolerance Network**  
Internet: [www.immunetolerance.org](http://www.immunetolerance.org)

**Integrated Islet Distribution Program**  
Internet: <http://iidp.coh.org>

## JDRF

26 Broadway, 14th Floor  
New York, NY 10004  
Phone: 1-800-533-CURE  
(1-800-533-2873)  
Fax: 212-785-9595  
Email: [info@jdrf.org](mailto:info@jdrf.org)  
Internet: [www.jdrf.org](http://www.jdrf.org)

## Acknowledgments

Publications produced by the Clearinghouse are carefully reviewed by both NIDDK scientists and outside experts. This publication was reviewed by Marlon Levy, M.D., medical director of the Pancreas and Islet Cell Laboratory, Baylor University Medical Center and Baylor All Saints Medical Center.

## National Diabetes Education Program

1 Diabetes Way  
Bethesda, MD 20814-9692  
Phone: 1-888-693-NDEP (1-888-693-6337)  
TTY: 1-866-569-1162  
Fax: 703-738-4929  
Email: [ndep@mail.nih.gov](mailto:ndep@mail.nih.gov)  
Internet: [www.ndep.nih.gov](http://www.ndep.nih.gov)  
[www.yourdiabetesinfo.org](http://www.yourdiabetesinfo.org)

The National Diabetes Education Program is a federally funded program sponsored by the U.S. Department of Health and Human Services' National Institutes of Health and the Centers for Disease Control and Prevention and includes over 200 partners at the federal, state, and local levels, working together to reduce the morbidity and mortality associated with diabetes.

You may also find additional information about this topic by visiting MedlinePlus at [www.medlineplus.gov](http://www.medlineplus.gov).

This publication may contain information about medications and, when taken as prescribed, the conditions they treat. When prepared, this publication included the most current information available. For updates or for questions about any medications, contact the U.S. Food and Drug Administration toll-free at 1-888-INFO-FDA (1-888-463-6332) or visit [www.fda.gov](http://www.fda.gov). Consult your health care provider for more information.

The U.S. Government does not endorse or favor any specific commercial product or company. Trade, proprietary, or company names appearing in this document are used only because they are considered necessary in the context of the information provided. If a product is not mentioned, the omission does not mean or imply that the product is unsatisfactory.

## National Diabetes Information Clearinghouse

1 Information Way  
Bethesda, MD 20892-3560  
Phone: 1-800-860-8747  
TTY: 1-866-569-1162  
Fax: 703-738-4929  
Email: [ndic@info.niddk.nih.gov](mailto:ndic@info.niddk.nih.gov)  
Internet: [www.diabetes.niddk.nih.gov](http://www.diabetes.niddk.nih.gov)

The National Diabetes Information Clearinghouse (NDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is part of the National Institutes of Health of the U.S. Department of Health and Human Services. Established in 1978, the Clearinghouse provides information about diabetes to people with diabetes and to their families, health care professionals, and the public. The NDIC answers inquiries, develops and distributes publications, and works closely with professional and patient organizations and Government agencies to coordinate resources about diabetes.

This publication is not copyrighted. The Clearinghouse encourages users of this publication to duplicate and distribute as many copies as desired.

This publication is available at  
[www.diabetes.niddk.nih.gov](http://www.diabetes.niddk.nih.gov).



National Institute of  
Diabetes and Digestive  
and Kidney Diseases

NIH Publication No. 13-4693  
September 2013



The NIDDK prints on recycled paper with bio-based ink.